Independent Risk Factors Predicting Gradual Onset Injury in 2824 Trail Running

Race Entrants: SAFER XVIII Study

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ABSTRACT:

Introduction: Trail running is characterized by elevation changes with uneven and varying running surfaces. Risk factors that may predict gradual onset running related injuries (GORRIs) in short distance trail running have not been explored. The objective was to determine risk factors that predict GORRIs in trail running race entrants who entered for mass community-based trail running events.

Methods: In this descriptive cross-sectional study, data were collected prospectively from a prerace medical screening questionnaire over 4 trail run events held annually. Using a Poisson regression model, runner demographics, race distance, running training/racing variables, history of chronic diseases (number of chronic diseases reported as a cumulative "chronic disease composite score"), and allergies were investigated to determine factors predicting self-reported GORRI history in the previous 12 mo.

Results: This study included 2824 race entrants (80% of entrants). The retrospective annual incidence for GORRIs was 13%. Independent risk factors predicting GORRIs were: longer race distance (*P*<0.0001), increasing chronic disease composite score (*P*=0.0012), and a history of allergies (*P*=0.0056). The lower limb (94%) was the main anatomical region of GORRIs, and soft tissue injuries accounted for most (83%) GORRIs. Common specific GORRIs were illiotibial band syndrome (22%), achilles tendon injury (10%), and hamstring injury (9%).

Conclusion: Independent risk factors predicting GORRIs among trail running entrants included longer race distance, a higher chronic disease composite score, and a history of allergies. This study has highlighted trail running race entrants at risk for sustaining GORRIs that could be targeted for future injury prevention interventions.

Keywords: chronic disease, running related injuries, incidence, epidemiology, off-road running, prerace medical screening

INTRODUCTION

Physical activity is associated with a reduced risk for developing chronic disease and premature all-cause mortality.¹ Evidence further suggests that participating in outdoor physical activity improves mental wellbeing.² Trail running involves running on off-road terrains in outdoor environments and is characterized by large elevation changes.³ Even though running has numerous proven physical and mental health benefits, it is still associated with a high risk for injury.⁴

The most common injuries described in running literature involve gradual onset running related injuries (GORRIs)^{4,5} as a result of low kinetic energy transfer over time causing tissue damage.⁶ Most studies only focus on marathon and ultramarathon running distances⁷⁻¹⁴ with limited information on GORRIs among trail runners participating in shorter distance trail run events.

In one study among ultra-distance trail runners, injury risk factors among elite runners included being more experienced runners, and runners with physical labor occupations. However, the authors did not investigate the medical history of participants. ²⁰ The prevalence of certain chronic diseases among endurance runners is up to 13%, ¹⁵ and chronic diseases are also associated with an increased risk for gradual onset injuries. ¹⁶⁻²⁰ Additionally, some medication used in the treatment of chronic diseases are associated with an increased risk for injury. ²¹⁻²⁷ The relationship between chronic diseases and risk of GORRIs has not been explored in trail runners.

The importance of investigating injury profiles and determining associated injury risk factors for GORRIs among this population is emphasized by the challenges faced during medical coverage at some trail running events.²⁸ These events can span over large geographical regions in remote settings where medical staff and runners are exposed to environmental hazards which include extreme weather, water crossings, insect-borne infections, and wildlife.^{28,29} In these settings, injured runners often receive delayed medical care due to the logistical challenges of providing emergency medical care in remote regions.^{28,29} A history of previous injury is a known injury risk factor among runners,^{30,31} therefore an attempt should be made to prevent injury in training period prior to race participation. For specific injury prevention strategies among short distance trail runners in the training period prior to race participation, we need an improved understanding of the injury profiles and associated injury risk factors for GORRIs in this population.

The main aim of this study was to determine risk factors that predict a history of GORRIs in trail running race entrants who entered for mass community-based trail running events. A secondary aim was to report the epidemiology and clinical characteristics of self-reported GORRIs among trail running race entrants.

METHODS

Study Design

A descriptive cross-sectional analysis of data collected prospectively at 4 annual trail running events.

Participants and data collection

The research ethics committee of the University of Cape Town (REC 009/2011 and REC 030/2013) approved the protocol and the research ethics committee of the University of Pretoria (REC 433/2015) approved the on-going data collection and subsequent analysis of the data.

This study forms part of the strategies to reduce adverse medical events for the exerciser (SAFER) studies—SAFER XVIII. Participants in this study were race entrants from the Two Oceans trail runs, a mass community-based trail running event in South Africa that is composed of a 10-km and a 22-km race. No qualification was required for either of the events. Entrants were defined as any runner registering for the races (registration typically opens 3–5 mo before the races) held annually over 4 y (2012–2015).

Online prerace medical screening

In this 4-y study period a compulsory prerace medical screening questionnaire was implemented for all race entrants. The prerace medical screening questionnaire was based on the European Association for Cardiovascular Prevention and Rehabilitation (EACPR) recommendations³² and consisted of the following main categories: history of cardiovascular disease (CVD), symptoms of CVD, risk factors for CVD, other chronic diseases, general prescription medication use, medication use during racing, injury and a past history of collapse during racing. The full detail of this online medical screening and implementation thereof has been described in previous studies.^{15,33} Entrants completing the screening were given the opportunity to consent to their data being used for research purposes.

In the prerace medical screening, entrants were asked the following specific question related to gradual onset injuries: "Do you or did you suffer from any symptoms of a chronic (no accident) running injury (muscles, tendons, bones, ligaments or joints) in the past 12 months or currently?". We defined these injuries as "GORRIs", as recommended by the 2020 international Olympic committee (IOC) consensus statement.⁶ For inclusion, an injury was defined as "An injury that is/was severe enough to interfere with running or require treatment e.g. use medication or require you to seek medical advice from a health professional". If the response to the previous question was "yes", entrants were required to complete additional questions related to the gradual onset running injury, including: past or current injury, anatomical region, body area, type of anatomical structure, severity and whether the injury was one of the more commonly known GORRIs.

Primary Outcome

The primary outcome of this study was a history of GORRIs in the past 12 mo among trail running race entrants. The following 3 categories of independent variables of interest as factors predicting GORRIs were explored: 1) demographics (sex and age groups) and race distance; 2) running training/racing variables (years as a recreational runner, average weekly training/running frequency in the last 12 mo, average weekly training/running distance in the past 12 mo, average training speed, race vs average training speed ratio); and 3) history of chronic disease (any risk factors for CVD, history of existing CVD, symptoms of CVD, endocrine disease, respiratory disease, gastrointestinal disease, nervous system/psychiatric disease, kidney/bladder disease, hematological/immune system disease, and cancer) and any allergies. We calculated a further variable, a chronic disease composite score (out of 10),

which is a continuous variable of the sum of an individual's answer to 10 questions related to the aforementioned history of chronic disease.

In the reporting on the outcomes in this manuscript, we used the terminology "prediction" instead of "association", based on recently published guidelines regarding clear goal setting in sports injury research. ³⁴In addition, we also reported the retrospective annual incidence (% runners: 95% CI) and frequency of injury characteristics (% of injuries) for anatomical region, body area, tissue type and common specific GORRIs. Injury severity was recorded as frequencies (%) of less severe (Grade I – only experience symptoms after exercise; and Grade II – experience symptoms during exercise but it does not interfere with exercise) and more severe (Grade III – experience symptoms during exercise that may interfere with training/competition; and Grade IV – may not be able to train/compete due to pain) injuries. ³⁵ More severe injuries were classified as those that interfered with the runner's ability to continue with training or racing.

Statistical Analysis

All race entrants' data were entered into Excel and then transferred into SPSS statistical software (version 25) and SAS (V.9.4) statistical analysis system. The binary-scaled dependent variable in the model was the response to the question related to GORRI, and entrants were coded as having a GORRI if they reported 1) a GORRI in the past 12 mo or 2) a current GORRI. Entrants could report more than one injury. Frequency analysis was performed for the descriptive data (% of all entrants; 95%CIs). For the risk factors, two groups were used (injured group n=338, control group n=2486), a Poisson distribution with a log link function was used and the *P*-values for a Type 3 GEE analysis were reported. All possible factors were first

explored in a univariate analysis. Using highly significant factors (*P*<0.001, due to the small sample size) from the univariate model, a multiple regression model was performed. Prevalence ratios (PR; 95% CIs) were reported and a final significance level of <0.05 was accepted.

RESULTS

Over the 4 annual events, 3547 runners entered and 2824 entrants (80%) gave consent for their data to be analyzed (10 km [n=1131] and 22 km [n=1693]). There were no significant differences between entrants consenting as study participants compared to all race entrants by sex, age groups or race distance (Table 1).

Table 1. Characteristics of all trail run race entrants and study participants

Characteristics	All trail run entrants (n=3547)	Study participants (n=2824)	P value ^b	
	$\%^a(n)$	$\%^a(n)$		
Sex				
Male	57 (2003)	57 (1597)	0.9485	
Female	44 (1544)	43 (1227)		
Age groups (y)				
≤30	30 (1073)	30 (857)	0.9124	
31-40	37 (1312)	36 (1022)		
41-50	23 (816)	24 (666)		
>50	10 (346)	10 (279)		
Race distance (km)				
10	41 (1463)	40 (1131)	0.3342	
22	59 (2084)	60 (1693)		

aPercentage of the total.

Annual incidence of GORRIs

In the previous 12 mo, 338 trail running race entrants reported a total of 349 GORRIs. Eleven (3%) of the 338 participants reported a second injury (total injuries, n=349) and 82 (24%) of

bP value—all trail run entrants vs entrants consenting as study participants.

the 338 participants suffered from a "current" injury at the time of completing the prerace screening questionnaire at race registration. The retrospective annual incidence of injuries in this study population was 13% (95%CI: 11 – 14).

Characteristics of GORRIs among trail running race entrants

The main anatomical region affected by GORRIs was the lower limb (94%: n=328), followed by the trunk (5%: n=16) and the upper limb (1%: n=2). The most common body areas affected by GORRIs were the knee (35%: n=123), followed by the shin/lower leg/calf (16%: n=55) and the thigh (11%: n=38) (Table 2).

Table 2. Anatomic region and specific body area of gradualonset running-related injuries among trail running race entrants (n=349)

Anatomic region	Body area	% (n)
Head and neck	Head	0(1)
Upper limb	Shoulder	0(1)
	Wrist	0(1)
Trunk		5 (16)
Lower limb	Hip/Groin/Pelvis	5 (18)
	Thigh	11 (38)
	Knee	35 (123)
	Achilles tendon	11 (37)
	Shin/Lower leg/Calf	16 (55)
	Ankle	6 (21)
	Foot	10 (36)
Unspecified		1(2)
Total		100 (349)

The most common specific GORRI was iliotibial band syndrome (ITBS) (22%: n=78), followed by achilles tendon injury (10%: n=35), hamstring injury (9%: n=30), calf muscle injury 7%: n=23) and foot/heel pain (5%: n=19) (Table 3).

Table 3. Frequency of common specific gradual-onset runningrelated injuries (12 mo prior to race entry) among trail running race entrants (n=349)

Common specific gradual-onset running-related injuries	% (n)	
Knee-iliotibial band syndrome	22 (78)	
Achilles tendon injury	10 (35)	
Hamstring injury	9 (30)	
Calf muscle injury	7 (23)	
Foot or heel pain	5 (19)	
Anterior knee pain/Patellofemoral pain	5 (16)	
Lower back pain	4 (15)	
Plantar fasciitis	4 (14)	
Hip muscle injury	3 (12)	
(including gluteus/buttock muscles)		
Shin splints (muscle/tendon)	3 (10)	
Shin splints (bone)	2 (8)	
Quadriceps muscle injury	1 (3)	
Lower leg compartment syndrome	1 (2)	
Other	24 (84)	
Total	100 (349)	

The frequency of Grade IV injuries (not able to train or compete due to injury) was 18% (n=63). The frequency of Grade III injuries was 33% (n=114), followed by Grade II (26%: n=90) and Grade I (23%: n=79). Slightly more severe GORRIs were reported as 51% (n=177) compared to the less severe injuries (48%: n=169).

Risk factors predicting a history of gradual onset injuries in trail running race entrants (Univariate analysis)

Runner demographics (sex, age group) and race distance

The overall prevalence of GORRIs (n=338) among trail running race entrants was 12% (95%CI: 11-14). The prevalence of GORRIs was not significantly different between males and females (PR=1.0, P=0.7722) and across age groups (P=0.1246). There was a higher prevalence of

GORRIs among trail running race entrants participating in the longer race distance (PR=1.8, P<0.0001) (Table 4).

Table 4. Number, prevalence, and PR of trail running race entrants with a history of GORRI by race distance, sex, and age group

Characteristics	Study participants (n=2824)	Study participants with a GORRI (n=338)		PR (95% CI)	P value
n Overall 2824	n	Prevalence (%; (95% CI)			
	2824	338	13 (11–14)		
Runner demographie	cs				
Sex					
Male	1568	184	12 (10-14)	1.0 (0.8-1.3)	0.7722
Female	1210	154	12 (11-14)		
Age groups (y)					
≤30	840	86	10 (8-13)		0.1246
31-40	1002	128	13 (11-15)	1.3 (1.0-1.7)	
41-50	663	92	14 (11-17)	1.4 (1.0-1.8)	
>50	273	32	11 (8-16)	1.1 (0.7-1.6)	
Race distance (km)					
10	1113	93	8 (7-10)	1.8 (1.4-2.3)	$< 0.0001^a$
22	1665	245	15 (13-17)		

GORRI, gradual-onset running-related injury; PR, prevalence ratio.

Running training/racing history

The number of years of recreational running (PR=1.1 per 5-unit increase; P=0.0014) and an increased average weekly training/running distance in the last 12 mo (PR=1.0 per 5-unit increase; P=0.0061) were associated with an increased PR for GORRIs (Table 5).

Missing data in 46 entrants.

^aStatistically significant.

Table 5. Prevalence and PR of trail running race entrants with a GORRI by training/racing history (unadjusted)

Running training/ racing history	Points in the continuous variable ^a	Trail run race entrants with a GORRI (n=338): prevalence (%; 95% CI)	PR (95% CI)	P value
Time as a recreational	3	11 (9-12)	5-unit increase	0.0014
runner (y)	6	11 (10-13)	1.1 (1.0-1.2)	
	13	13 (12-14)		
Average weekly	2	11 (9-13)	2-unit increase	0.0610
training/ running	3	12 (11-13)	1.1 (1.0-1.3)	
frequency in the last 12 mo (times·wk ⁻¹)	4	13 (11–14)		
Average weekly	15	11 (10-12)	5-unit increase	0.0061^{a}
training/running	25	12 (11-13)	1.0 (1.0-1.1)	
distance in the past 12 mo (km)	40	13 (12–15)		
Average training speed	9	12 (10-13)	1-unit increase	0.5046
(km-h ⁻¹)	11	12 (11-14)	1.0 (1.0-1.1)	
	13	13 (11-14)		
Race vs training speed	0.5	14 (12-17)	0.5-unit increase	0.0590
ratio (RS/TS ^b)	1.0	11 (9-13)	1.0 (0.9-1.1)	
	1.5	8 (5-13)		

GORRI, gradual-onset running-related injury; PR, prevalence ratio.

History of chronic disease and allergies

The results of trail running race entrants with a GORRI by history of chronic disease and allergies is shown in Table 6.

Table 6. Number, prevalence, and PR of trail running race entrants with a GORRI by history of chronic disease and allergies (unadjusted)

Characteristics Study participants (n=2824) n		Race entrants with a GORRI (n=338)		PR (95% CI)	P value
	n	Prevalence (%; 95% CI)			
History of chronic					
disease					
Chronic disease					
composite score (0)-10) ^a				
0	_	_	11 (10-12)	2-unit increase	0.0004^{b}
2	-	-	19 (15-23)	1.7 (1.4-2.2)	
4	_	-	32 (21-49)		
History of allergies					
Any allergies					
Yes	322	65	19 (15-24)	1.7 (1.3-2.2)	0.0008^{b}
No	2455	273	11 (10-13)		
Missing	47	0			

GORRI, gradual-onset running-related injury; PR, prevalence ratio.

aStatistically significant.

^bRace speed (km·h⁻¹) vs training speed (km·h⁻¹) ratio = race speed/training speed; a value > 1 is a faster average race speed compared to average training speed, and a value <1 is a slower average race speed compared to average training speed.

The composite number of 10 chronic diseases for an individual (continuous variable, therefore no number of participants in the groups).

^bStatistically significant.

A higher chronic disease composite score was associated with a higher prevalence of GORRIs among trail running race entrants (PR=1.7; P=0.0004) in a "dose-dependent" fashion (Figure 1). For every two additional chronic diseases, the prevalence of GORRIs increased 1.7 times. Notably, the confidence intervals widened as the score increased, due to the number of entrants with higher composite scores decreasing. A history of any allergies (PR=1.7, P=0.0008) was associated with a higher PR for GORRIs among trail running race entrants.

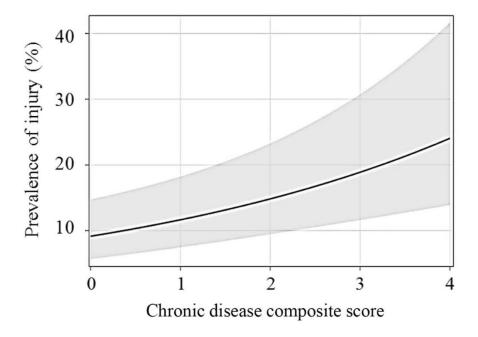


Figure 1.The relationship between the prevalence of gradual-onset running-related injuries and the number of chronic diseases (chronic disease composite score) (shaded area is 95% CI). Wide confidence intervals are indicative of the small sample size at that score.

Independent risk factors predicting a history of GORRIs in trail running race entrants (Multiple Regression Analysis)

Independent risk factors predicting a history of GORRIs in trail running entrants were longer race distance (PR=1.9, P<0.0001), a higher chronic disease composite score (PR=1.6, P=0.0012), and a history of any allergies (PR=1.6, P=0.0056) (Table 7).

Table 7. Independent risk factors that predict a history of GORRIs in the past 12 mo (multiple regression analysis)

	Runners with a GORRI % (95% CI)	PR (95% CI)) P value	
Race distance (km)		-		
10	9 (7-11)	1.9 (1.5-2.4)	< 0.0001°	
22	17 (15-20)			
History of chronic disease				
Chronic disease composite score ^b				
0	12 (10-14)	2-unit increase:	0.0012^a	
2	19 (15-23)	1.6 (1.3-2.1)		
4	30 (20-46)			
History of allergies				
Any allergies				
Yes	18 (14-22)	1.6 (1.2-2.0)	0.0056^{a}	
No	11 (10-13)			

Adjusted for age and sex.

DISCUSSION

In our study, runners entering for the longer trail run had a higher prevalence of self-reported GORRIs. Runners entering longer race distances are usually more experienced and train at higher weekly running distances in comparison to entrants of shorter race distances. Among Greek trail runners, increased running experience was associated with a higher risk of injury. ¹³ We found similar results in our univariate analysis indicating that increased years of running were associated with a higher PR of a GORRI. Our univariate analysis also indicated that an increased average weekly running distance was associated with a higher prevalence of a GORRI. Future studies using larger sample sizes may identify running experience and weekly running distance as independent risk factors predicting a history of GORRIs.

We showed that a higher chronic disease composite score predicted a history of GORRIs. Specifically, for every two additional chronic diseases present the prevalence of GORRIs increased 1.6 times in a "dose-dependent" fashion. This is an intriguing finding. The prevalence of chronic disease among endurance runners has been reported at between 2% to 13% and 16% of runners have at least one risk factor for CVD. 15 Studies confirm that a

GORRI, gradual-onset running-related injury; PR, prevalence ratio.

^aStatistically significant.

^bThe composite number of 10 chronic diseases for an individual (continuous variable).

variety of chronic diseases, which affect various organ systems, are associated with an increased risk for gradual onset injuries. For example, diabetes mellitus, hypercholesteremia, and obesity are associated with a higher risk of tendinopathy, and chronic obstructive pulmonary disease (COPD) is associated with an increased risk for bone stress injuries. 19,20

Another consideration is that the medications used in the treatment of chronic diseases may also be associated with an increased risk for injury.²¹⁻²⁷ There are reports that drug-induced tendinopathy is associated with the use of fluoroquinolones,²⁴ statins,^{22,25} corticosteroids,²¹ aromatase-inhibitors,²⁷ and isotretinoin.²³ A higher risk for tendon ruptures²¹ and osteoporosis²⁶ are reported with the use of corticosteroids, while isotretinoin increased the risk for developing enthesopathy.²³ The relationship between the medication dosage and adverse effects is not well quantified in the use of corticosteroids,²⁶ but the adverse effects of statins appear to be dose-dependent. Finally, certain medication interactions are associated with increased tendon toxicity³⁶ and combinations of medications are a further risk factor for developing a toxic tendinopathy.³⁷

The cross-sectional nature of our study limits our ability to establish a cause-effect relationship between the chronic disease composite score and injury risk. These findings do suggest that not only the presence of chronic disease, but also the choice of medication used in treatment, medication dosage, and medication interactions need to be explored as risk factors for GORRIs in future studies.

We also showed that a history of allergies predicted a history of GORRIs. Trail runners participate in various outdoor settings where they are exposed to a variety of potential allergens. Trail running is an endurance sport, and it is well established that a history of

allergies is common in endurance athletes. ^{15,38} We can only speculate on the possible reasons for the association between allergies and GORRI. Again, both the allergy itself and the medication used to treat allergies may be mechanisms responsible for the increased risk of injury. Anti-histamines are commonly used to treat allergies, but have side-effects such as fatigue and drowsiness. ³⁹ If this medication is used during training and racing, acute fatigue can alter lower extremity muscle strength, postural control, and ankle joint position sense, which may increase injury risk. ⁴⁰ Future research should explore the relationship between allergies, the medication used to treat allergies and GORRIs.

This is the only study to report the annual incidence (13%) of GORRIs among short distance trail running race entrants, therefore we could not compare our results to any current literature. Our results show that the lower limb (94%) is the most commonly injured anatomical region and this is a similar finding to that previously reported among longer distance trail runners.^{8,9,11,13,14,41} In our study, the knee was the most common body area for GORRIs (35%) which is much higher compared to Dutch trail runners (18%).⁴¹ In downhill running, the knee is exposed to increased flexion angles during load absorption and redistribution, and this may contribute to the higher prevalence of knee injuries.⁴² The lower frequency of knee injuries reported among Dutch trail runners⁴¹ may be related to a difference in the trail running landscape in the Netherlands with minimal elevation changes.

Our results indicated that soft tissue accounted for 82% of all injured tissue types. The specific tissues involved were muscle (33%), followed by tendon (30%) and ligament (18%), and these findings are similar to those reported in Dutch trail runners (muscle=28%, tendon=24%, ligament=7%).⁴¹ In ultra-distance trail runners similar injured tissue types were found with tendon (36%), ligament (43%), and muscle (21%).¹¹ However, we note that in the

Italian trail running study, acute injuries were included, specifically a high number of ankle sprains. Therefore, we cannot strictly compare our data to that study.¹¹

Finally, we show that 51% of GORRIs are severe enough to interfere with training or competition (Grade III and IV). Even though Grade IV injuries were the least frequently reported (18%), it is of concern if a trail runner cannot continue with running due to pain, especially during training/racing in remote regions where medical evacuation is challenging.²⁸ We cannot compare this finding to other studies because there is substantial variation in the definitions of injury severity in the trail running literature,^{8,41} which restricts our ability to compare results.

LIMITATIONS

This study has several limitations. We cannot determine a cause-effect relationship between any of the identified risk factors due to the cross-sectional nature of the study. All the injury and training data are self-reported and could have been affected by recall bias. Owing to recall bias, we could not accurately determine the study participants' actual running exposure on trails. The diagnosis of injuries could not be verified. Lastly, we acknowledge that many other factors (eg, elevation change, running surface, individuals' level of conditioning, intrinsic lower limb biomechanics, footwear etc.) may also be associated with the risk for developing GORRIs, but could not be explored in our study. Future studies are needed to explore the causal relationship between the risk factors and GORRIs among short distance trail running race entrants.

CONCLUSION

Independent risk factors that predict a history of GORRIs among short distance trail running

entrants include longer race distance, a higher chronic disease composite score, and history

of any allergies. Specifically, for every two additional chronic diseases present the prevalence

of GORRIs increased by 1.6 times in a "dose-dependent" fashion. Our results highlight trail

running race entrants at risk for sustaining GORRIs that could be targeted for future injury

prevention interventions.

Author contribution:

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REFERENCES

- 1. Lee D-C, Brellenthin AG, Thompson PD, Sui X, Lee IM, Lavie CJ. Running as a key lifestyle medicine for longevity. *Prog Cardiovasc Dis.* 2017;60(1):45-55.
- 2. Thompson Coon J, Boddy K, Stein K, Whear R, Barton J, Depledge MH. Does participating in physical activity in outdoor natural environments have a greater effect on physical and mental wellbeing than physical activity indoors? A systematic review. *Environ Sci Technol.* 2011;45(5):1761-72.
- 3. Scheer V, Basset P, Giovanelli N, Vernillo G, Millet GP, Costa RJS. Defining off-road running: a position statement from the ultra sports science foundation. *Int J Sports Med.* 2020.
- 4. Messier SP, Martin DF, Mihalko SL, Ip E, DeVita P, Cannon DW, et al. A 2-year prospective cohort study of overuse running injuries: the runners and injury longitudinal study (TRAILS). *Am J Sports Med.* 2018;46(9):2211-21.
- Lopes AD, Hespanhol Júnior LC, Yeung SS, Costa LO. What are the main runningrelated musculoskeletal injuries? A Systematic Review. Sports Med. 2012;42(10):891-905.
- 6. Bahr R, Clarsen B, Derman W, Dvorak J, Emery CA, Finch CF, et al. International Olympic committee consensus statement: methods for recording and reporting of epidemiological data on injury and illness in sport 2020 (including STROBE extension for sport injury and illness surveillance (STROBE-SIIS)). *Br J Sports Med*. 2020;54(7):372-89.

- 7. Graham SM, McKinley M, Chris CC, Westbury T, Baker JS, Kilgore L, et al. Injury occurrence and mood states during a desert ultramarathon. *Clin J Sport Med.* 2012;22(6):462-6.
- 8. Krabak BJ, Waite B, Schiff MA. Study of injury and illness rates in multiday ultramarathon runners. *Med Sci in Sports Exerc.* 2011;43(12):2314-20.
- 9. Scheer BV, Murray A. Al Andalus Ultra Trail: an observation of medical interventions during a 219-km, 5-day ultramarathon stage race. *Clin J Sport Med.* 2011;21(5):444-6.
- McGowan V, Hoffman MD. Characterization of medical care at the 161-km Western States Endurance Run. Wilderness Environ Med. 2015;26(1):29-35.
- 11. Vernillo G, Savoldelli A, La Torre A, Skafidas S, Bortolan L, Schena F. Injury and illness rates during ultratrail running. *Int J Sports Med.* 2016;37(7):565-9.
- 12. Costa R, Snipe R, Camões-Costa V, Scheer V, Murray A. The impact of gastrointestinal symptoms and dermatological injuries on nutritional intake and hydration status during ultramarathon events. *Sports Med Open.* 2016;2(1):1-14.
- 13. Malliaropoulos N, Mertyri D, Tsaklis P. Prevalence of injury in ultra trail running. *Human Movement*. 2015;16(2).
- Hoffman MD, Stuempfle KJ. Muscle cramping during a 161-km ultramarathon:
 comparison of characteristics of those with and without cramping. Sports Med Open.
 2015;1(1):24-.

- 15. Schwabe K, Schwellnus M, Swanevelder S, Jordaan E, Derman W, Bosch A. Leisure athletes at risk of medical complications: outcomes of pre-participation screening among 15,778 endurance runners SAFER VII. *The Phys and Sportsmed*. 2018;46(4):405-13.
- 16. Ranger TA, Wong AMY, Cook JL, Gaida JE. Is there an association between tendinopathy and diabetes mellitus? A systematic review with meta-analysis. *Br J Sports Med.* 2016;50(16):982-9.
- 17. Abboud JA, Kim JS, Abboud JA, Kim JS. The effect of hypercholesterolemia on rotator cuff disease. *Clin Orthop Relat Res.* 2010;468(6):1493-7.
- 18. Aicale R, Tarantino D, Maffulli N. Overuse injuries in sport: a comprehensive overview. *J Orthop Surg and Res.* 2018;13(1):309.
- 19. Hattiholi J, Gaude GS. Prevalence and correlates of osteoporosis in chronic obstructive pulmonary disease patients in India. *Lung India*. 2014;31(3):221-7.
- 20. Nayyar N, Sood RG, Sarkar M, Tomar A, Thakur V, Bhoil R. Prevalence of osteoporosis and osteopenia in stable patients of chronic obstructive pulmonary disease in Sub-Himalayan region of Himachal Pradesh, India. *J Family Med Prim Care*. 2017;6(3):595-9.
- 21. Blanco I, Krähenbühl S, Schlienger RG. Corticosteroid-associated tendinopathies: an analysis of the published literature and spontaneous pharmacovigilance data. *Drug Saf.* 2005;28(7):633-43.

- 22. Hayem G. Statins and muscles: what price glory? Joint Bone Spine. 2002;69(3):249-51.
- 23. Kirchgesner T, Larbi A, Omoumi P, Malghem J, Zamali N, Manelfe J, et al. Drug-induced tendinopathy: from physiology to clinical applications. *Joint Bone Spine*. 2014;81(6):485-92.
- 24. Mandell L, Tillotson G. Safety of fluoroquinolones: an update. *Can J Infect Dis.* 2002;13(1):54-61.
- 25. Marie I, Noblet C. [Drug-associated tendon disorders: after fluoroquinolones ... here are statins!]. *Rev Med Interne*. 2009;30(4):307-10.
- 26. Rice JB, White AG, Scarpati LM, Wan G, Nelson WW. Long-term systemic corticosteroid exposure: a systematic literature review. *Clin Ther.* 2017;39(11):2216-29.
- 27. Vuillemin V, Guerini H, Bard H, Morvan G. Stenosing tenosynovitis. *J Ultrasound*. 2012;15(1):20-8.
- 28. Hoffman M, Pasternak A, Rogers I, Khodaee M, Hill J, Townes D, et al. Medical services at ultra-endurance foot races in remote environments: medical issues and consensus guidelines. *Sports Med.* 2014;44(8):1055-69.
- 29. Laskowski-Jones L, Caudell MJ, Hawkins SC, Jones LJ, Dymond CA, Cushing T, et al. Extreme event medicine: considerations for the organisation of out-of-hospital care during obstacle, adventure and endurance competitions. *Emerg Med J.* 2017;34(10):680-5.

- 30. Dallinga J, Van Rijn R, Stubbe J, Deutekom M. Injury incidence and risk factors: a cohort study of 706 8-km or 16-km recreational runners. *BMJ Open Sport Exerc Med.* 2019;5(1):e000489-e.
- 31. Van Der Worp MP, De Wijer A, Van Cingel R, Verbeek ALM, Nijhuis-Van Der Sanden MWG, Staal JB. The 5- or 10-km Marikenloop run: a prospective study of the etiology of running-related injuries in women. *J Orthop Sports Phys Ther.* 2016;46(6):462-70.
- 32. Borjesson M, Serratosa L, Carre F, Corrado D, Drezner J, Dugmore DL, et al. Consensus document regarding cardiovascular safety at sports arenas: position stand from the European association of cardiovascular prevention and rehabilitation (EACPR), section of Sports Cardiology. *Eur Heart J.* 2011;32(17):2119-24.
- 33. Schwellnus M, Swanevelder S, Derman W, Borjesson M, Schwabe K, Jordaan E. Prerace medical screening and education reduce medical encounters in distance road races:

 SAFER VIII study in 153 208 race starters. *Br J Sports Med.* 2019;53(10):634-9.
- 34. Nielsen RO, Simonsen NS, Casals M, Stamatakis E, Mansournia MA. Methods matter and the 'too much, too soon' theory (part 2): what is the goal of your sports injury research? Are you describing, predicting or drawing a causal inference? *B J Sports Med.* 2020:bjsports-2020-102144.
- 35. Taunton JE, Ryan MB, Clement DB, McKenzie DC, Lloyd-Smith DR, Zumbo BD. A prospective study of running injuries: the Vancouver Sun run "in training" clinics. *Br J Sports Med.* 2003;37(3):239-44.

- 36. Ward NC, Watts GF, Eckel RH. Statin toxicity. Circ Res. 2019;124(2):328-50.
- 37. Bolon B. Mini-review: toxic tendinopathy. *Toxicol Pathol.* 2017;45(7):834-7.
- 38. Robson-Ansley P, Howatson G, Tallent J, Mitcheson K, Walshe I, Toms C, et al.

 Prevalence of allergy and upper respiratory tract symptoms in runners of the London marathon. *Med Sci Sports Exerc.* 2012;44(6):999-1004.
- 39. Randall KL, Hawkins CA. Antihistamines and allergy. Aust Prescr. 2018;41(2):42-5.
- 40. Verschueren J, Tassignon B, De Pauw K, Proost M, Teugels A, Van Cutsem J, et al. Does acute fatigue negatively affect intrinsic risk factors of the lower extremity injury risk profile? a systematic and critical review. *Sports Med.* 2020;50(4):767-84.
- 41. Hespanhol Junior LC, van Mechelen W, Verhagen E. Health and economic burden of running-related injuries in Dutch trailrunners: a prospective cohort study. *Sports Med.* 2017;47(2):367-77.
- 42. Park S-K, Jeon H-M, Lam W-K, Stefanyshyn D, Ryu J. The effects of downhill slope on kinematics and kinetics of the lower extremity joints during running. *Gait Posture*. 2019;68:181-6.

FIGURE LEGEND

Figure 1: The relationship between the prevalence of GORRIs and the number of chronic diseases (chronic disease composite score) (shaded area is 95% CI). Wide confidence intervals are indicative of the small sample size at that score